1186 New Insights Into the Causes of Acute Coronary Events

Wednesday, April 1, 1998, Noon–2:00 p.m.
Georgia World Congress Center, West Exhibit Hall Level
Presentation Hour: 1:00 p.m.–2:00 p.m.

1186-128 Anti-oxidized-LDL Antibodies as a Possible Cause of Inflammation in Unstable Angina

F. Summaria, C. Monaco, G. Niccoli, R. Teoli, G. Bellomo[1], C. Perugini[1], M. Bagnati[1], A. Buffon, G. Liuzzo, G. Caligiuri, F. Crea, A. Maseri. *Catholic University, Rome, Italy; [1]Department of Medical Sciences, University of Torino, Novara, Italy*

Background: Several studies have shown an activation of inflammatory cells encluding lymphocytes in patients (pts) with unstable angina (UA). However the observation that elevated levels of acute phase proteins such as C-reactive protein (CRP) are present in 50–60% of pts with UA suggests that the inflammatory response is associated to instability of angina in an subset of pts.

Methods and Results: In order to establish whether the cause of inflammatory response in these pts is associated to raised levels of oxidized-LDL antibodies (Ox-LDL Ab) we studied 10 pts with UA and elevated CRP (> 3 mg/dl; G1) and 6 pts with UA and low levels of CRP (< 3 mg/dl; G2). In particular we measured serum levels of Ab (IgM and IgG) to oxidized LDL (LDL oxidized with Cu++ for 2, 4, 18 hours).

Ox-LDL Ab	2 h		4 h		18 h	
	IgM	IgG	IgM	IgG	IgM	IgG
G1	0.231	0.093	0.307	0.136	0.291	0.161
G2	0.144	0.072	0.182	0.080	0.142	0.179
p (G1 vs. G2)	0.02	0.02	0.007	0.03	0.007	0.004

2 h, 4 h, 18 h = oxidation times

Conclusion: The inflammatory response detected by elevated CRP levels in patients with Unstable Angina is associated with Ox-LDL Ab. Therefore Ox-LDL Ab may be a trigger of the inflammatory response commonly observed in patients with Unstable Angina.

1186-129 Increase of Interleukin-1Ra and Interleukin-6 Levels During the First Two Days of Hospitalization Is Associated With Raised Risk of In-hospital Coronary Events in Unstable Angina

G. Liuzzo, G. Fantauzzi, F. Ginnetti, G. Caligiuri, V. Rizzello, D.J. Angiolillo, C. Colizzi, C.A. Dinarello, L.M. Biasucci, A. Maseri. *UCSC, Rome, Italy; University of Colorado, Denver, CO, USA*

Background: IL-1Ra (marker of IL-1β and TNF-α levels) and IL-6 are cytokines associated with an adverse outcome in sepsis and in other acute illness and major inducers of acute phase proteins. In turn, acute phase protein levels have been associated with short and long-term prognosis in ischemic heart disease.

Methods: To assess IL-1Ra and IL-6 time course and relation with prognosis in unstable angina (UA) we measured their levels in 43 patients (pts) with UA (Braunwald's class III B) on hospital admission and after 48 hours (h) of full medical therapy (including i.v. heparin and i.v. nitrates).

Results: Pts were grouped according to the presence of in-hospital events (death, myocardial infarction, refractory angina): 26 pts had in-hospital events (G1), and 17 had an eventful course (G2). Although G1 had more ischemic episodes then G2, their number and lenght was not statistically different between the two groups IL-1Ra (ng/ml) and IL-6 (pg/ml) levels (median and range) are shown in the table.

	G1		G2	
	entry	48 hours	entry	48 hours
IL1Ra	0.35 (0.1–0.85)	0.43 (0.1–1.23)*	0.18 (0.1–1.4)	0.18 (0.1–0.82)
IL-6	7.30 (3–22.9)	9.50 (3–47.5)*	4.70 (0.1–12.6)†	0.94 (0.1–10.4)

IL-1Ra: $p < 0.01$ G1 vs G2 at entry; IL-6: $p < 0.05$ G1 vs G2 at entry; G1: * $p < 0.01$ 48 h vs entry; G2: † $p < 0.01$ entry vs 48 h.

Conclusion: Our study demonstrates that IL1-Ra and IL-6 levels are elevated on admission and increase further at 48 h, in spite of full medical therapy in pts with UA and in-hospital events, as commonly observed in acute inflammatory illness with adverse outcome. Conversely, pts with an uneventful in-hospital course have significantly lower levels of IL-1Ra and IL-6 on admission and no increase at 48 h. Our data may open new avenues to novel therapeutic approaches in unstable angina.

1186-130 Extensive Coronary Calcification Is a Strong Predictor of Chronic Coronary Events

J. Shemesh, A. Tenenbaum, C.I. Stroh, E.Z. Fisman, M. Motro. *Chaim Sheba Medical Center, Sackler School of Medicine, Tel-Aviv University, Tel-Aviv, Israel*

The effect of coronary calcification (CC) on the natural history of coronary artery disease is not well defined. This study aimed to investigate the predictive value of extensive CC by double helical CT (DHCT), on the future development of coronary events.

Methods: We followed 802 patients with coronary artery disease or multiple coronary risk factors, mean age 62 ± 7 (507 men) who underwent DHCT scanning, along a mean period of 24 ± 9 months. The registered cardiac events were divided into 2 categories: acute events (sudden death, acute MI or new unstable angina) and chronic events defined as an elective procedures due to stable AP or positive perfusion tests (coronary angiography, PTCA or CABG). Patients were divided into 3 groups according to the total coronary calcium score (TCS): Absence – TCS = 0, mild – TCS < 300 and extensive – TCS ≥ 300.

Results: The incidence of events (acute and chronic) during the follow up period was as follows:

	TCS = 0 (n = 213)	TCS < 300 (n = 432)	OR (CI)	TCS ≥ 300 (n = 157)	OR (CI)
Acute	6 (2.8)	18 (4.2)	1.6 (0.6–4.4)	4 (2.6)	1.0 (0.2–3.6)
Chronic	1 (0.5)	18 (4.2)	9.4 (1.3–169.6)	45 (28.3)	63.5 (13.1–999)

Data presented as number (%) of patients who suffered events. OR = age adjusted odds ratio. CI = 95% confidence interval

There were no significant differences in the incidence of acute events among the study groups, whereas extensive CC was a strong predictor of future cardiac interventions.

In Conclusion: The presence of extensive coronary calcification on DHCT is highly predictive for chronic but not acute coronary events.

1186-131 Oxidized Low Density Lipoprotein (OxLDL) Step-up May Trigger Acute Coronary Events

S. Ehara, M. Ueda, T. Naruko, H. Itagane, K. Haze, H. Itabe, T. Takano, Y. Tsukamoto, A.E. Becker. *Osaka City General Hospital, Osaka City University Medical School, Osaka, Japan*

Background: There is increasing evidence that acute coronary synromes relate to recent activation of the inflammatory processes associated with atherosclerotic plaques. Oxidized low density lipoprotein (OxLDL) is considered to play a key role in the genesis of these inflammatory processes. Recently, a sandwich ELISA method for measurement of plasma OxLDL has been developed by using two monoclonal antibodies. To elucidate whether an increase in the blood levels of OxLDL could be involved, we have measured the plasma levels of OxLDL in patients with acute myocardial infarction (AMI), unstable angina (UAP) and stable angina pectoris (SAP). Moreover, we have measured the OxLDL blood level in an autopsied patient, who die of AMI and, in addition, have studied the presence of OxLDL in the culprit lesion.

Methods and Results: Plasma OxLDL levels were measured in 37 patients (AMI: 12, UAP: 14, SAP: 11), and in 18 control subjects. In patients with AMI, blood samples were obtained within 24 hours after onset. Plasma OxLDL levels in patients with AMI were significantly ($P < 0.05$) higher than in patients with UAP or SAP (AMI:2.43 ± 1.85, UAP: 0.99 ± 0.69, SAP: 0.70 ± 0.36, ng/5 μgLDL protein, mean ± SD). Serum levels of total cholesterol, HDL, LDL, and triglyceride did not differ among these groups. An autopsied patient revealed an increased blood level of OxLDL, and immunohistochemically the culprit coronary lesion of this patient contained abundant OxLDL-positive foam cells.

Conclusions. This is the first study to demonstrate that the plasma level of OxLDL is directly related to the seventy of the acute coronary syndromes.

1186-132 Relationship Between Clinical Efficacy of Oral Roxithomycin and IgG Titers for *Chlamydia Pneumoniae* in the ROXIS Pilot Study

E. Gurfinkel, G. Bozovich, A. Daroca, B. Livellara, E. Beck, Branco Mautner. *On behalf of the ROXIS Study Group; Favaloro Foundation, Durand Hospital, Italiano Hospital, Buenos Aires, Argentina*

Background: Chalmydia pneumoniae has been related to atherogenesis and plaque instability. However, there is lack of evidences of the effect of specific antibiotics and serum markers of infection and inflammation.

Method: We evaluated the effect of roxithomycin in a cohort of 202 consecutive patients admitted to the Coronary Unit because of acute non-Q-wave events. Subjects were randomly allocated to either roxithromycin 300 mg